Lentiginosis, Deafness and Cardiac Abnormalities*

R. E. CRONJE, M.B. B.CH. UNIV. RAND, M.R.C.P. EDIN AND A. FEINBERG, M.B. CH.B. UNIV. PRET.,
Department of Paediatrics, University of Pretoria and Cardiac Unit, H.F. Verwoerd Hospital, Pretoria

SUMMARY

Three members of a family with features of the 'leopard' syndrome are described. The important findings were generalized lentigo, deafness, and cardiac and electrocardiographic abnormalities. Progressive obstructive cardiomyopathy and arrhythmias are features of the condition which may be present, and are potentially life-threatening.

S. Afr. Med. J., **47**, 15 (1973).

The association between generalized lentigo, deafness and cardiac abnormalities has become widely recognized. The name 'leopard' syndrome has been given to the condition, to serve as a mnemonic to the main features of the syndrome. The 'leopard' syndrome in its complete form consists of deafness, multiple lentigines, mental and physical retardation, ocular, cardiac and electrocardiographic (ECG) defects and abnormal genitalia.[1] It may be a familial disorder and is then inherited as an autosomal dominant of variable penetrance. Sporadic cases have also been described. It appears that the sporadic form of the disease is more severe and leads to early disability and death. The familial form is milder.

The cardiac lesion commonly consists of hypertrophic obstructive cardiomyopathy of either ventricle or abnormalities of the ECG.[2] The obstructive lesion may be progressive and cause cardiac failure. The ECG features include conduction abnormalities, such as left hemiblock, combinations of bundle-branch block, and arrhythmias such as complete heart block or paroxysmal tachycardia.[3]

Defects of the organ of Corti may be responsible for the deafness, which is sensineural in type. Lentigines are small, dark brown spots appearing either congenitally or shortly after birth, and increasing in number with age. They should be differentiated from freckles (ephelides), which increase in number on exposure to sunlight, and appear at a later age. Ocular abnormalities have included hypertelorism and retinal pigmentation.[2]

Undescended testes, delayed menarche and other abnormalities of the genitalia have been described in approximately half the cases, and the suggestion has been made that the more severe cases would be unable to bear children, even if they lived long enough.

CASE REPORTS

Case 1

This was the propositus. He complained only of attacks of palpitation. Eleven years of age, he was well built, and of normal intelligence, mass and height. His skin was covered with lentigines 1 - 5 mm in diameter, especially over the trunk, with the face and lower legs largely spared (Fig. 1).

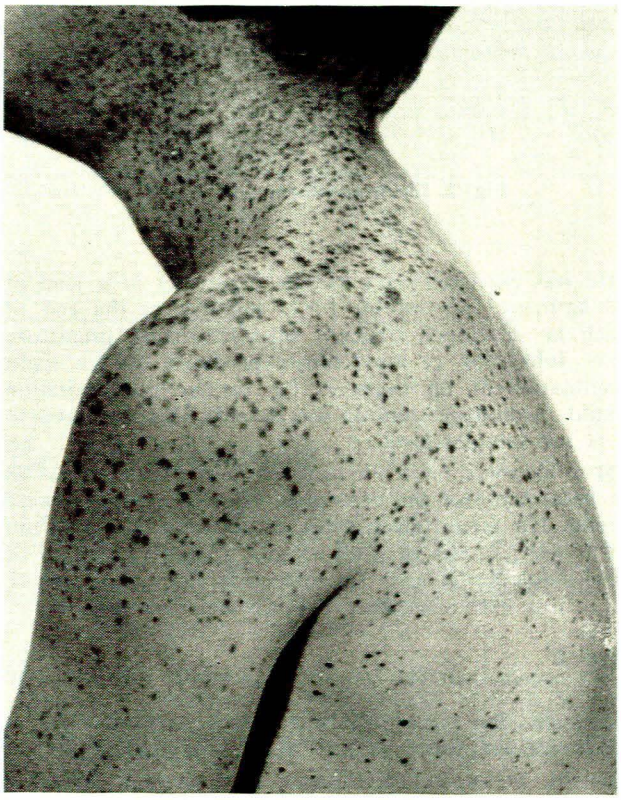

Fig. 1. Lentigenes of case 1.

He was not deaf. Genitalia were normal. He was not cyanotic. There were no signs of cardiac failure. Blood pressure was 120/80 mmHg in the arms. All pulses were palpable and normal in rate and volume. Occasional premature beats were present. The heart was not clinically enlarged and no abnormal impulses were palpable. The heart sounds were normal. A grade 3 out of 6 ejection murmur was best heard over the 3rd interspace on the left sternal margin.

On roentgen examination the pulmonary conus appeared to be slightly prominent. The electrocardiogram showed a P-R interval of 0,2 seconds, right axis deviation, right

* Date received: 7 July 1972.

ventricular hypertrophy, and uncommonly deep S waves in V1 - V6 (Fig. 2). An anti-clockwise loop was present in the frontal plane of his vector cardiogram.

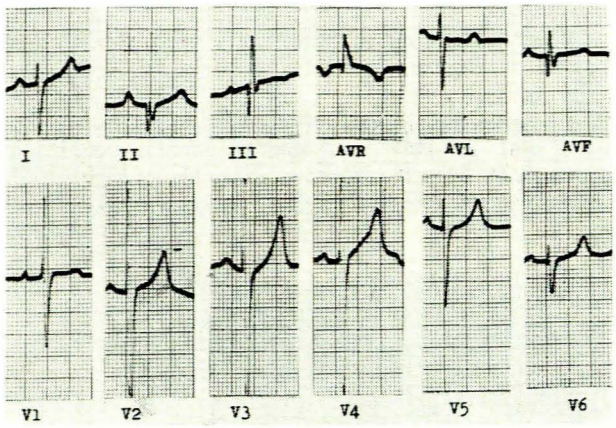

Fig. 2. Electrocardiogram of case 1.

He was exercised on a bicycle ergometer at a load of 600 kg-metres per minute for 5 minutes, at the end of which he developed frequent supraventricular premature beats. Inhalation of amyl nitrite produced only a slight accentuation of his murmur. On cardiac catheterization a mild pulmonary stenosis was found. This appeared to be at sub-valvular level.

Skin biopsy showed an increase in the melanocytes in the basal layer of the epidermis. His chromosomes were normal. His serum electrolytes, blood urea, blood count, and blood proteins were all normal. Urinary excretion of 5-OH-indole-acetic acid and catecholamines was normal.

Case 2

This was the father. He had no symptoms. He had a sensineural deafness, and generalized lentigo (Fig. 3).

Height, mass, and intelligence were normal. Winging of the scapula and a marked tortuosity and prominence of the main arteries in the arm with locomotor brachialis was present. A grade 2 out of 6 blowing, early to mid-systolic murmur, was audible over the cardiac apex. On ECG prominent S waves were present on leads V1 - V5 (Fig. 4).

Case 3

This was the brother. He had a severe degree of sensineural deafness, generalized lentigo, a grade 2 out of 6 ejection murmur over the pulmonary area of the heart, and deep S waves on electrocardiographic leads V1 - V6 (Fig. 5). His height, mass, intelligence and genitalia were normal.

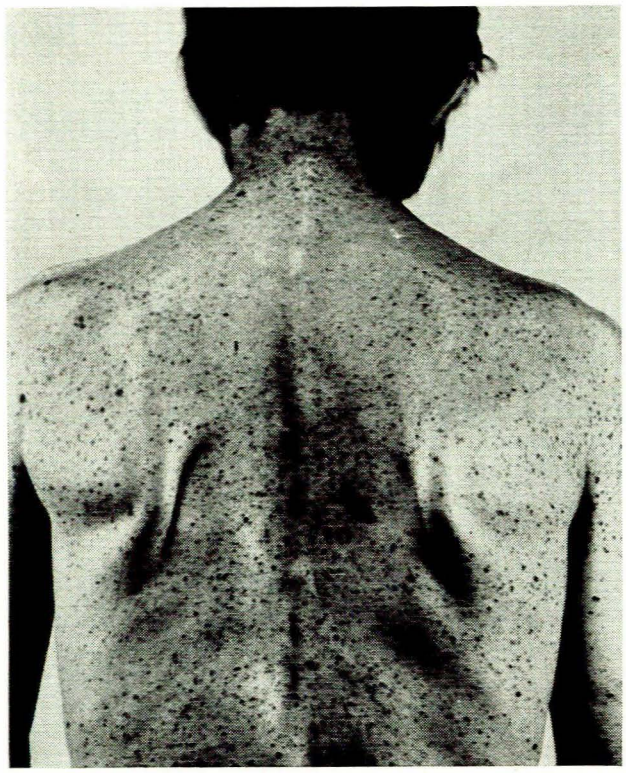

Fig. 3. Lentigines and winging of scapulae in case 2.

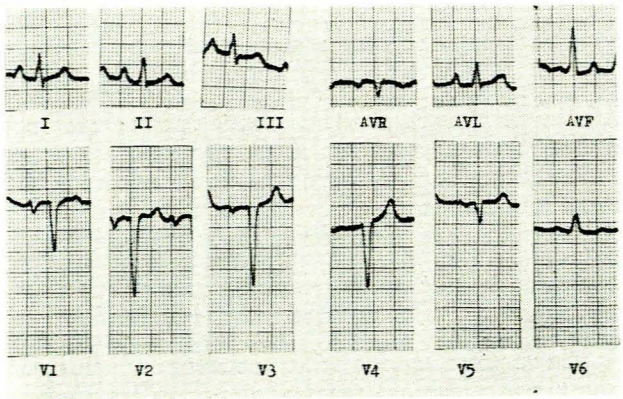

Fig. 4. Electrocardiogram of case 2.

DISCUSSION

The association between deafness and disturbance of cardiac conduction and between pigmented skin lesions and cardiac abnormalities, has been well described. Should a patient present with multiple lentigines and/or familial sensineural deafness, then the possibility of a heart lesion being present should be investigated. The cardiac abnormality may take the form of a life-threatening arrhythmia, or a progressive hypertrophic obstructive cardiomyopathy.[2]

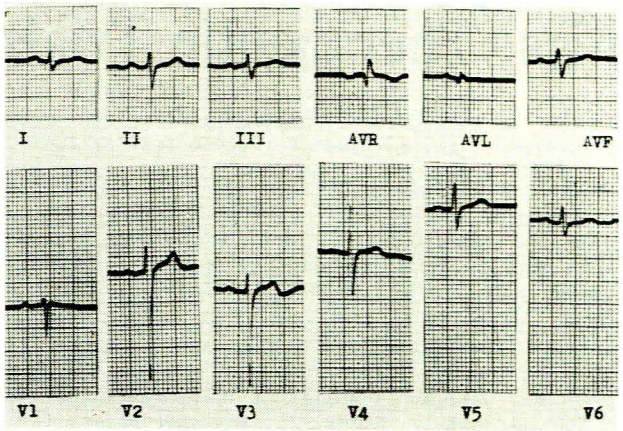

Fig. 5. Electrocardiogram of case 3.

These patients should therefore be followed-up, even if they show no signs of a cardiomyopathy at first examination. The mode of inheritance of the condition in the family described would fit in with that of an autosomal dominant with variable penetration. The father was the only affected member of a family of nine children. Two of his children were affected.

The pathogenesis of the condition is unknown. Polani and Moynahan[4] have suggested that this syndrome could be attributed to an anomaly of neural crest elements. The sympathetic nervous system, noradrenaline, serotonin and corticosteroids, are closely linked to the regulation of melatonin and melanocytes, as well as pigment metabolisms.[5]

Further discussion of the pathogenesis will be mere speculation, until more investigations are carried out.

We wish to thank the Superintendent of H. F. Verwoerd Hospital for permission to publish.

REFERENCES

1. Pickering, D., Laski, B., MacMillan, D. C. and Rose, V. (1971): Arch. Dis. Childh., **46**, 85.
2. Somerville, J. and Bonham-Carter, R. E. (1972): Brit. Heart J., **34**, 58.
3. Smith, R. F., Pulicichio, L. U. and Holmes, A. V. (1970): Amer. J. Cardiol., **25**, 501.
4. Polani, P. E. and Moynahan, E. J. (1972): Quart. J. Med., **41**, 205.
5. Wolstenholme, G. E. W. and Knight, J. (1971): *The Pineal Gland*. Edinburgh: Churchill Livingstone.